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EXAMINER	
SRIVASTAVA, KAILASH C	

ART UNIT	PAPER NUMBER
1657	

MAIL DATE	DELIVERY MODE
11/26/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/580,507	PARISSENTI ET AL.	
	Examiner	Art Unit	
	Dr. Kailash C. Srivastava	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-5 and 12-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 12-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/03/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The response, amendments and remarks filed 20 August 2008 to Office Action mailed 26 June 2008 is acknowledged and entered.

Claims Status

2. Claims 6-11 and 18 have currently been cancelled.

3. Claims 1, 12 and 15 have currently been amended.

4. Claims 1-5 and 12-17 are currently pending.

Restriction/Election

5. Election with traverse of Group I invention encompassing Claims 1-5 "drawn to a method to determine a sequence to administer multiple chemotherapeutics to kill cancerous cells to reduce drug-resistance induction in a patient and Claims 12-14 drawn to a composition comprising a plurality of isogenic cell lines obtained from a single cancerous tumor filed 20 August 2008 to Office Action mailed 26 June 2008 is acknowledged and entered.

Examiner is puzzled with applicants' traversal of election of invention because in the election/ restriction requirement in the Office Action mailed 26 June 2008, there was no requirement to elect between the method Claims in Group Ia and Composition Claims 12-17 in Group Ib, rather the election was required of a Group among Groups I-III. Groups Ia and I were separately listed to only distinguish between the method Claims and Composition Claims because the current application is a 371 of PCT/CA04/02039.

Regarding the species election among different cell Lines as listed in Claim 12, said election of species requirement in he Office Action cited *supra* is hereby withdrawn on the basis of telephone interview between the Examiner and the applicants' representative on 20 August 2008 and explanation given by the Applicants' Representative (See Interview Summary Mailed 08/26/2008).

Accordingly, the restriction requirement is deemed proper and is made FINAL.

6. The elected invention in Claims 1-5 and 12-17 is examined on merits.

Priority

7. Claim for foreign priority under 35 U.S.C. §119(a-d) to PCT/CA04/02039 filed 26 November 2004 is acknowledged.

8. Claim for domestic priority under 35 U.S.C. §119(e) to U.S. Provisional Application Serial Number 60/525,479 filed 26 November 2003 is acknowledged.

Information Disclosure Statement

9. The Information Disclosure Statement (i.e., IDS) filed 06 November 2006 has been made of record, considered and duly initialed/signed forms PTO 1449 or equivalent is enclosed.

Objection to Specification

10. The currently presented specification is objected to because Line one of first page of specification, in its present form does not properly cite the application priority data. It is requested that the first line of the first page of the specification indicate that the instant application Claims priority to Canadian PCT Application, as follows:

"This application Claims Priority to PCT/CA04/02039 filed 26 November 200, which Claims Priority to U.S. Provisional Application Serial Number 60/525,479 filed 26 November 2003."

Objection to Claims

11. Claims 1-5 and 12-17 objected to because of the following informalities:

- Claims 1-5 and 12-17 are objected to because of the recitation, "derived" in Claims 1a, 12 and 15 in relation to the context of subject material described in said Claims. "Derived "is a terminology that means , e.g., relating to a characteristic that was changed from one generation to the next, or in phylogenetics, derived members of a group diverged after another member (or subgroup of members) had already diverged (http://www.google.com/search? Google+Search&aq. =f&oq=, Printed 11/21/2008). Thus, said term does not clearly define how similar a material should be to the base material to be called a derivative, i.e. the term does not define the metes and bounds of the claimed subject matter. Examiner suggests replacing the term, "derivative" with the term, "obtained".

- Claims 2-5 and 16-17 are objected to because at Line one of each one of the cited Claims, before the word "wherein" a --, -- should be inserted.

Objection to Abstract

12. The abstract of the disclosure is objected to because of a verbose term at Line 4. The term, "patent" deems to be "patient". Appropriate correction is required because Abstract should correctly represent the invention for which protraction is being sought...

Claim Rejections - 35 U.S.C. § 112

Second Paragraph Rejections

13. The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> ***The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.***

14. Claims 1-5 and 12-17 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- Recitation, " sequence" at Line 1 in the preamble of each of Claims 1 and 15 as currently presented, renders said Claims incomprehensible, unclear and vague since the metes and bounds for said recitation are unclearly defined. The metes and bounds for said claim need to be clearly defined.

- Recitation, "strains" at Line 1 of each of Claims 1a, 12 and 15a; recitation "progeny strains" at Line 1 of each of Claims 1a and 15a and recitation "strain" in Claims 1c, 3, 12 and 15c-17 as currently presented, renders said Claims incomprehensible, unclear and vague since the art-recognized meaning of word "strain" is two cells having different genotype or phenotype or both". Thus, as presented currently, the metes and bounds for said recitation are unclearly defined. The metes and bounds for said claim need to be clearly defined or the art-known terminology "clone" may be applied.

- At Line 1 of each of Claims 1c and 15c, the limitation is "order". There is insufficient antecedence basis for said limitation in said claims, because at Line 1 of the preamble of each of Claims 1 and 15, the limitation is "sequence". Appropriate correction is required.

- The recitation, "undesired" in Claim 15 is similar to the word "preferably" and renders said Claim confusing, unclear, vague and therefore indefinite. It is not clear whose undesireness is being referred to, and further, how can one determine with clarity and accuracy when the "undesireness" is to be exercised and what are the metes and bounds of the term, "undesired". Metes and bounds for the recitation, "undesired' should be defined.

All other claims directly or indirectly depend from the rejected claim, e.g., Claim 1 and are, therefore, also rejected under 35 U.S.C. §112, 2nd paragraph for the reasons set forth above.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness Rejections set forth in this Office action:

> ***(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.***

16. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § *103*(c) and potential 35 U.S.C. §*102*(f) or (g) prior art under 35 U.S.C. § 103(a).

17. Claims 1-5 and 12-17 are rejected under 35 U.S.C. §103(a) as obvious over the combined teachings from Alli et al. (2002. Effect of Stathmin on the Sensitivity to Antimicrotubule Drugs in Human Breast Cancer, Cancer Research ,Volume 62, Pages 6864–6869) in view of Pardee et al (US Patent 6,664,288 B1).

Claims recite human breast cancer isogenic cell lines obtained from the same breast tumor, an *in vitro* method to assay an order in which multiple chemotherapeutic drugs for killing cancerous cells to reduce the induction of drug cross-resistance in a patient should be administered to said patient, wherein the selected lead chemotherapeutic drug expresses a reduced capacity to induce cross resistance in a patient against one or more known anticancer drugs. The Claims further recite all of the drugs having the

ability to kill cancerous cells of the same selected tumor type. Furthermore, the claimed methods involve determining an order to administer multiple types of cytotoxic drugs for killing undesired cells to reduce the indication of drug cross-resistance in the cells. The assay is based on IC_{50} value of said cytotoxic anticancer chemotherapeutic drugs.

Regarding Claims 1-5 and 12-17, Alli et al., teach a number of human breast cell line clones (Page 6864, Column 2, Lines 37-50) and further teach an assay applying 96 well plate assay to determine the IC_{50} value for each of the chemotherapeutic drugs (Page 6865, Column 1, Lines 41-55). The assay criterion was overexpression of stathmin on the panel of human breast cancer cells as a function of different doses of test chemotherapeutic drugs (Abstract, Column 1, Lines 14-25). Said chemotherapeutic drugs were: camptothecin, doxorubicin, paclitaxel and inelastic (Page 6864, Column 2, Lines 57-58). Note further, biogenic cell lines over-expressing stathmin were generated and applied for said assay to determine the binding of paclitaxel and vinblastine (Page 6865, Column 2, Lines 49-52). Data on stathmin overexpression as a function of decreased binding in a number of panels of breast cancer cells of paclitaxel (Figure 3) and of vinblastine (Figure 4) as well as comparative data on sensitivity of each of paclitaxel and vinblastine (Figure 5) and IC_{50} values on the sensitivity of doxorubicin and camptothecin (Table 1) at different doses of said latter two chemotherapeutic drugs Clearly indicate that the cell resistance was highest to doxorubicin and least to vinblastine with camptothecin and paclitaxel in middle but cells were more sensitive to paclitaxel than to camptothecin. Also, the viability of said cells was determined as percentage of control by dividing the absorbance of each treated well by the average of the untreated, or carrier treated controls. Please note camptothecin represents both topotecan and irinotecan (See Wikipedia, http://en.wikipedia.org/wiki/camptothecin", Printed 11/19/2008). Despite showing the resistance order of a variety of human breast cell line panels to anticancer chemotherapeutic drugs, wherein cells were least sensitive to doxorubicin and most sensitive to vinblastine (comparison of date shown in Figure 5 and Table 1). Alli et al., however are silent regarding the order to administer the anticancer chemotherapeutic drugs to a patient.

Pardee et al., teach an *in vitro* assay with a variety of human breast cancer cell lines. In said assay, to exponentially growing human breast cancer cell lines in the 6 well-plates the known amounts of test chemotherapeutic drugs were directly administered. In said assay, the sensitivity of a variety of anticancer chemotherapeutic drugs consisting of the group comprising β-lapachone, camptothecin (topotecan and irinotecan are analogues of camptothecin), epirubicin, mitoxantrone, taxol (i.e., paciltaxel) and vinblastine was determined (Column 6, Lines 56-64; Column 15, Lines 45-56; Column 15, Line 66 to Column 16, Line 9). Based on the data obtained, the order of administering said drugs was

determined. The lead chemotherapeutic drug to be administered is β-lapachone and next one to follow is paclitaxel (Column 18, Lines 15-32). Even though Pardee et al., do not explicitly disclose least cross resistance of said chemotherapeutic drugs because of administering said chemotherapeutic drugs to an individual, the claims are obvious from the teachings of cited prior art reference because administration of said chemotherapeutic drugs in said order would intrinsically function as claimed (i.e., demonstrate least cross resistance to said drugs because said prior art composition is comprised of same components (i.e., chemotherapeutic drugs and breast cancer cell line panels) and is being administered in the same way as the claimed chemotherapeutic drugs (See e.g., *In re Best*, 195 USPQ 430, 433-CCPA 1977).

One having ordinary skill in the art at the time of claimed invention would have been motivated to combine the teachings from Alli et al., with the beneficial teachings from Pardee et al.; because Pardee et al., teach the order of administering chemotherapeutic drug and further intrinsically teach least cross resistance of said chemotherapeutic drugs. The actual order of the component in the prior art surface (i.e., composition) may not be the same as instantly claimed. However, the adjustment of particular conventional working components/ conditions (e.g., orders of administration, concentration etc.), is deemed merely a matter of judicious selection and routine optimization of a result-effective parameter which is well within the purview of the skilled artisan. In view of the fact that the applicants' invention also recites breast cancer cell line panels and same chemotherapeutic drugs as are disclosed in prior art teachings; applicants' invention is obvious over the teachings of Examiner-cited prior art references.

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings from Alli et al., with the beneficial teachings from Pardee et al.; because Pardee et al., teach the order of administering chemotherapeutic drug and further intrinsically teach least cross resistance of said chemotherapeutic drugs. It is also *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." (*In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (citations omitted)).

From the teachings of the references cited *supra*, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

18. No Claims are allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Kailash C. Srivastava whose telephone number is (571) 272-0923. The examiner can normally be reached on Monday to Thursday from 7:30 A.M. to 6:00 P.M. (Eastern Standard or Daylight Savings Time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Jon Weber can be reached at (571)-272-0925 Monday through Thursday 7:30 A.M. to 6:00 P.M. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding may be obtained from the Patent Application Information Retrieval (i.e., PAIR) system. Status information for the published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (i.e., EBC) at: (866)-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Dr. Kailash C Srivastava/
Examiner, Art Unit 1657

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22 November 2008
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